Research Article

The effect endometrial scratching done during diagnostic hysteroscopy on improving the pregnancy rates in women with recurrent Intracytoplasmic sperm injection (ICSI) failure – El-Minia experience

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Abstract
Objectives :- Hysteroscopic endometrial scratching is a simple, minimally invasive, low cost procedure that may enhance biochemical and molecular changes that increase pregnancy rates specially cases of recurrent ICSI failure. **Methodology:-** 40 patients of recurrent ICSI failure for variable time interval and variable number of failed ICSI cycles were randomly divided into two groups for the study groups, 20 patient for each group. Hysteroscopic endometrial scratching done in cases of group I the (intervention group) during diagnostic hysteroscopy before ICSI cycle at day 21 (the time of starting pituitary down regulation). Cases of group II (controlled group) will do diagnostic hysteroscopy before ICSI cycle without endometrial scratching, then the cases followed to asses implantation rate, biochemical serum pregnancy test, pregnancy rate, abortion rate and incidence of multiple pregnancy in both groups. **Results:-** Hysteroscopic endometrial scratching increased pregnancy rate in cases of recurrent ICSI failure during routine diagnostic hysteroscopy by 15 % in group I than group II and not affecting abortion rate .
Conclusion :- Hysteroscopic endometrial scratching could be used in all cases of recurrent ICSI failure during routine diagnostic hysteroscopy as it increase pregnancy rate without increase the abortion rate.
Keywords: Endometrial scratching, Hysteroscopy, ICSI, ICSI failure.

Introduction
Endometrial scratching is a simple, minimally invasive, low cost procedure that may affect biochemical and clinical pregnancy rates, the endometrium is gently 'scratched' using the hystroscope or a thin catheter (a fine, flexible, sterile, plastic tube) which is passed through the cervix (Li l et al., 2011).[5]

Endometrial scratching alters endometrial gene expression. In particular, it up-regulates the mucin-1 transmembrane, laminin a4, integrin a 6 (ITGa6), matrix metalloproteinase 1, bladder transmembrane, anal uroplakin IB and phospholipase A2 genes, all of which are thought to be involved in facilitating the preparation of the endometrium for embryo implantation via the regulation of cellular proliferation, differentiation and adhesion (Qin et al., 2003; Zhou et al., 2008; Kalma et al., 2009;Almog et al., 2010; Dekel et al., 2010; Dekel et al., 2012; Granot et al., 2012)[6,7,8,9,10,11,12]

The aim of this study
To assess the role of hysteroscopic endometrial Scratching on pregnancy rate in women undergo ICSI.

Patient and methods
A prospective case control Study was conducted in Minia Infertilty Research Center at the University hospital and other private infertility centers at El minia governorate from the period between the 1st of January 2014 to the 1st of January 2016 for evaluation 40 women undergo ICSI to evaluate the role of endometrial scratching in pregnancy rate in women with ICSI

Ethical permission was sought from a Local Research Ethic Committee, According to the hospital protocol. Eligible women will receive oral and written information. Patients consented for data retrieval for research purpose before the time of the procedure after ensuring the confidentiality,

Inclusion criteria:

- Age: 20_35y
- All patients who suffering from recurrent ICSI failure due to various causes except cases in the exclusion criteria.

Exclusion criteria:

- Failure to do hysteroscopy.
- Intrauterine cavitary lesions and endo-metrial lesions which may affect the implantation and pregnancy rate such as submucous fibroid, uterine congenital anomalies and intrauterine adhesions.

Women without endometrial abnormalities with recurrent ICSI failure were allocated into two groups; the scratching group was consisted of patients who underwent endometrial scratching during routine diagnostic hysteroscopy and the control group was consisted of patients who underwent only diagnostic hysteroscopy without endometrial scratching.

A total of 40 women with recurrent ICSI failure fulfilling the inclusion criteria aged 20-35 years old were randomly divided into two groups through closed envelope randomization.

1- Study (the intervention) group (20 patients):-

In the intervention group (Group I), hysteroscopic endometrial scratch will be performed once during the luteal phase of the cycle prior to subsequent ICSI cycle . The scratch will be done on day 21 or 5 days after a positive urine ovulation test .

Procedure of hysteroscopy and endometrial scratching:

In the theatre, Patients put in a lithotomy position, sterilization was performed with the presence of good source of light, the procedure was carried out using office hysteroscopy - containing operative channel as usual. The endometrium is scratched by small grasper at the fundus and at the posterior wall gently. The procedure took approximately 15minutes to complete. Post procedure antibiotics were given.

2- Control group (20 patients):-

They will do diagnostic hysteroscopy which done as a routine procedure in cases of recurrent ICSI failure as first group but without performing endometrial scratching.

Follow up:

Serum pregnancy test (Quantitative type) done after 2 week of embryo transfer. When a woman has become pregnant (women with positive pregnancy test), she will undergo ultrasounds at approximately 6 weeks and 10–12 weeks of gestation, after which she will continue prenatal care to record abortions. Multiple pregnancies also recorded. Comparative study was done for both groups and results presented in tables and statistically analyzed.

Statistical analysis

Analysis of data was done using SPSS (statistical program for social science version 12) as follows:

- Description of quantitative variables as mean, SD and range.
- Description of qualitative variables as number and percentage.
- Unpaired t-test was used to compare two groups as regard quantitative variable in parametric data (SD<25% mean.

Chi—square test was used to compare tow groups as regard qualitative variable

Results

Table 1: Shows Demographic data and base line characteristics of the patients.

	Group I (study group) (n=20)	Group II (control group) (n=20)	P value
Age **Range** **Mean ± SD**	 (21-34) 25.36 ± 3.44	 (20-35) 26.72 ± 4.48	0.092
Marriage duration **Range** **Mean ± SD**	 (5-12) 4.38 ± 1.93	 (6-14) 4.26 ± 1.87	0.753
Previous marriage	0 (0%)	0 (0%)	-------
BMI **Range** **Mean ± SD**	 (19-27) 21.52 ± 2.38	 (18-30) 22.34 ± 3.03	0.136

Table 2: Number of failed ICSI cycles and number of previous diagnostic hysteroscopy in previous ICSI cycles

	Group I (Study group) (n=20)	Group II (Control group) (n=20)	P value
Number of failed ICSI cycles in patients (mean ±SD)	2.4 ±0.4	2.9 ±0.07	0.45
Number of patients with previous diagnostic hysteroscopy in previous ICSI cycles (mean ±SD)	1.5 ±0.2	1.3 ±0.5	0.35

Table 3: Shows the Follow up of the cases for 3 months after ICSI .

	Group I (Study group) (n=20)	Group II (Control group) (n=20)	P value
Pregnancy rate	10 (50%)	6 (35%)	0.028*
Visible pulsation at 5ws by TVS	20 (100%)	17 (%)	------
Abortion rate in early pregnancy before completed 13ws	0 (0%)	4 (20%)	0.004*
Incidence of multiple pregnancy	5 (25%)	3 (15 %)	

Discussion

This is a prospective case control study where 40 patients of recurrent ICSI failure divided randomly into two groups, study and control groups.

All patients followed up for 3 months to detect rate of pregnancy for both groups. Our results show increased pregnancy rate among endometrial scratching group at 50% while only 35% in the control group

got pregnant which considered significantly different. These results are similar to those obtained by ebrahim et al., 2013[13] who concluded that the pregnancy rate was significantly higher in the endometrial injury group compared to the control group [17/114 (14.9%) vs. 6/103 (5.8%) (OR: 2.83 95% CI: 1.07-7.49, p=0.03]. Also our results are similar to that of maged etal 2016[14] who found that the cumulative PR was significantly higher in group S (39%) compared to group C (18.2%). The PR in group S was significantly higher compared to that in group C at the second and third trials.

Zouh et al.,[7] who also investigated the possibility that local injury to the endometrium in COH cycle improves the incidence of embryo implantation in IVF-ET, ET and found that local injury to the endometrium during a COH cycle improved the rates of embryo implantation, clinical pregnancy, and live birth in ART.

However, our results against those obtained by Karimzade[15] and colleagues, They evaluated the effect of local injury to the endometrium on the day of oocyte retrieval on implantation and pregnancy rates in assisted reproductive cycles. The results demonstrated that local injury to the endometrium on the day of oocyte retrieval disrupted the receptive endometrium and had a negative impact on implantation in IVF cycles.

As regard abortion rate, no significant difference was found between the two groups concerning the abortion rate (p=0.4). These results are in agreement with Barash et al.,[16] who found that pre-implantation endometrial scratching doubled the rate of getting pregnancy and not affecting the abortion rate.

The mechanisms by which the endometrial scratching could be beneficial for increased pregnancy rate is it might enhance endometrial decasualization and potentiate rapid growth of endometrial cells.

Also it enhances a massive secretion of different cytokines and growth factors which are beneficial for embryo implantation , Also, the last mechanism is synchronization of endometrial and embryo development. Mirkin et al.,[17] reported that COH cycles resulted in different structural and functional changes in comparison to natural cycles, including histological advancement, pinopodes maturation advancement, and steroid receptor down-regulation

Conclusion

Hysteroscopic endometrial scratching could be used in all cases of recurrent ICSI failure during routine diagnostic hysteroscopy as it increase pregnancy rate without increase the abortion rate. The results of the current study need to be confirmed by further studies on other populations.

Endometrial local injury could be considered as one of the treatment options for selected UI couples whose infertility most likely due to implantation failure.
This simple, easy, and cost effective procedure is worth considering in infertile couples especially in younger couples with shorter duration of infertility before complex treatments.

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